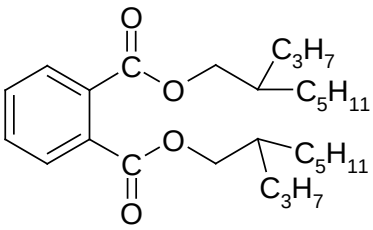
FACT SHEET HBM value for DPHP			
Substance name	**Di-2-propylheptylphthalate; 1,2-Benzenedicarboxylic acid bis(2-propylheptyl) ester**		
Parameter	**Value / Descriptor**	**Dimension**	**Comments**
HBM Guide value			
Guide value I (HBM-I, precautionary value)	**Children: 1 Adults: 1,5**	**mg/L**	**Morning urine/spot urine (rounded value)**
Year of issue	2014		
status	final		
General Information			
CAS No	53306-54-0		
IUPAC name	Bis(2-propylheptyl) phthalate		
Molar mass substance	446,7	g/mol	
HBM-parameter	oxidized monoester oxo-MPHP and OH-MPHP		specific metabolites, limit of quantification: 0,25 – 0,30 µg/L [1]
Molar mass metabolites	320,4 and 322,4; mean: 321,4	g/mol	
Database			
Tolerable intake (TDI, RfD or comparable)			RfD: 0,1 mg/(kg KG · d), based on human equivalent $BMDL_{10}$ for effects on thyroid gland (Bath et al., 2014) [2]; value given for further information, not used as POD by the HBM commission
Key study / Author(s) (Year)	BASF (1995a)		selected as key study by the HBM Commission
Species	Wistar rats		
Route/type of study	oral/ subchronic		OECD 408
Study length (Exposure duration)	3 month		
Exposure pattern	with feed		
Critical endpoint/ effect	effects on thyroid gland and pituitary gland (BfR 2011) [3]		
POD_{HBM-I}	**40**	**mg/(kg bw · d)**	**NOAEL**
Assessment factors			**used by the HBM Commission**
Dose-response assessment factor	n.a.		
Severity of effect	-		
Adjusted exposure duration factor (time scaling)	n. a.		Oral study
Adjusted study length factor	2		Subchronic → chronic

Route-to-route extrapolation factor	n. a.		
Adjusted absorption factor	n. a.		
Interspecies factor	10		
Intraspecies factor	10		
Sensitive population factor	1		
Other adjustment factors Quality of whole database	-		
Total assessment factor (TAF)	**200**		
Kinetik terms			
Factor for metabolic conversion (Fue)	0,24 [4]		48h, oxo-MPHP and OH-MPHP
Proportion molar mass metabolites to molar mass DPHP	0,72		321,4 / 446,7
Urine volume	Children: 0,03 Adults: 0,02	L/(kg bw · d)	
Result (Calculation)			
POD_{HBM-I}/TAF (TDI analog)	0,2	mg/(kg bw · d)	40/200
kinetic extrapolation and HBM value calculation [5]	200 x 0,72 x 0,24 = 34,56 children: 1152 (= HBM-I) adults: 1728 (= HBM-I)	µg/(kg bw · d) µg/L morning urine	tolerable amount OH-MPHP + oxo-MPHP in the urine = TDI analog x (molecular weight metabolites/molecular weight DPHP) x Fue consideration of urine volume, Children: division by 0,03 Adults: division by 0,02

Remarks: According to the evaluation of the German Bundesinstitut für Risikobewertung (BfR) [3] the technical DPHP consists of approx. 81% Di-2-Propylheptylphthalate, approx. 18% 2-Propylheptylphthalate, 2-Propyl-4-methylhexylphthalate and 1% Di-2-Propyl-4-methylhexylphthalate.
In pursuance of Wittasek and Angerer [6] children seem to have a more effective oxidative metabolism of phthalates compared to adults. Those age specific differences in the human metabolism have not been investigated for DPHP. Likewise no data concerning the correlation between the amount of body burden and the excretion of metabolites exist.

Rationale

1,2-benzenedicarboxylic acid, di-2-propylheptyl ester (DPHP) is used as plasticizer for the manufacturing of plastics, mainly polyvinylchloride (PVC).
A subchronic feeding study with rats revealed a NOAEL (No Observed Adverse Effect Level) of 40 mg/(kg bw · d), which can be used as point of departure (POD) for the derivation of a HBM-I value. Application of a total assessment factor of 200 leads to an estimation of 200 µg/kg bw as tolerable daily intake of DPHP (TDI analog). On the basis of the results of metabolism studies with humans it is possible to calculate back from the tolerable daily intake of DPHP to the tolerable concentration of specific metabolites in urine. Thus a HBM-I value of 1 mg/L morning urine for children and 1,5 mg/L morning urine for adults was derived for the sum of the oxidized monoesters oxo-MPHP and OH-MPHP, which were identified as robust and conclusive biomarkers for DPHP. Currently available data on concentrations of oxo-MPHP and OH-MPHP in urine samples of the German Environmental Specimen Bank indicate exposure levels clearly below the HBM-I value. Further studies will show if a plateau is already reached or if an increase in the body burden of DPHP and its metabolites will occur as a result of its increasing use as alternative to other phthalates.
The HBM Commission deliberated the HBM value for HBCD on the basis of a dossier prepared by the Fraunhofer Institute (FhG; O. Licht, I. Mangelsdorf and J-U. Voss) on behalf of the Federal Environment Agency.

Literature

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